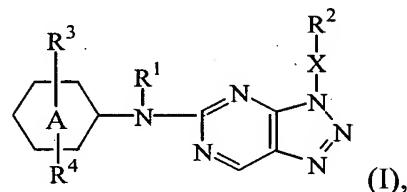


**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A compound of formula



a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereochemically isomeric form thereof, wherein

ring A represents phenyl, pyridyl, pyrimidinyl, pyridazinyl or pyrazinyl;

R<sup>1</sup> represents hydrogen; aryl; formyl; C<sub>1-6</sub>alkylcarbonyl; C<sub>1-6</sub>alkyl; C<sub>1-6</sub>alkyloxycarbonyl;

C<sub>1-6</sub>alkyl substituted with formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxycarbonyl,

C<sub>1-6</sub>alkylcarbonyloxy; or C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkylcarbonyl optionally substituted with

C<sub>1-6</sub>alkyloxycarbonyl;

X represents a direct bond; -(CH<sub>2</sub>)<sub>n3</sub>- or -(CH<sub>2</sub>)<sub>n4</sub>-X<sub>1a</sub>-X<sub>1b</sub>-;

with n<sub>3</sub> representing an integer with value 1, 2, 3 or 4;

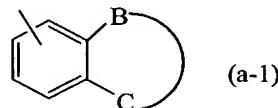
with n<sub>4</sub> representing an integer with value 1 or 2;

with X<sub>1a</sub> representing O, C(=O) or NR<sup>5</sup>; and

with X<sub>1b</sub> representing a direct bond or C<sub>1-2</sub>alkyl;

R<sup>2</sup> represents C<sub>3-7</sub>cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle

containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula



wherein -B-C- represents a bivalent radical of formula

-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>- (b-1);

-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -	(b-2);
-X <sub>1</sub> -CH <sub>2</sub> -CH <sub>2</sub> -(CH <sub>2</sub> ) <sub>n</sub> -	(b-3);
-X <sub>1</sub> -CH <sub>2</sub> -(CH <sub>2</sub> ) <sub>n</sub> -X <sub>1</sub> -	(b-4);
-X <sub>1</sub> -(CH <sub>2</sub> ) <sub>n'</sub> -CH=CH-	(b-5);
-CH=N-X <sub>1</sub> -	(b-6);

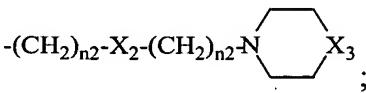
with X<sub>1</sub> representing O or NR<sup>5</sup>;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

wherein said R<sup>2</sup> substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy; C<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkyl-carbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; C<sub>2-6</sub>alkenyl or C<sub>2-6</sub>alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; polyhalo-C<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; C<sub>1-6</sub>alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyl-oxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; polyhaloC<sub>1-6</sub>alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; C<sub>1-6</sub>alkylthio; polyhaloC<sub>1-6</sub>alkylthio; C<sub>1-6</sub>alkyloxycarbonyl; C<sub>1-6</sub>alkylcarbonyloxy; C<sub>1-6</sub>alkylcarbonyl; polyhaloC<sub>1-6</sub>alkylcarbonyl; cyano; carboxyl; NR<sup>6</sup>R<sup>7</sup>; C(=O)NR<sup>6</sup>R<sup>7</sup>;

-NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>; -NR<sup>5</sup>-C(=O)-R<sup>5</sup>; -S(=O)<sub>n1</sub>-R<sup>8</sup>; -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; -S-CN; -NR<sup>5</sup>-CN; aryloxy; arylthio; arylcarbonyl; arylC<sub>1-4</sub>alkyl; arylC<sub>1-4</sub>alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted with at least

one substituent selected from R<sup>9</sup>; or 

with n2 representing an integer with value 0, 1, 2, 3 or 4;

with X<sub>2</sub> representing O, NR<sup>5</sup> or a direct bond;

with X<sub>3</sub> representing O, CH<sub>2</sub>, CHO, CH-N(R<sup>5</sup>)<sub>2</sub>, NR<sup>5</sup> or

N-C(=O)-C<sub>1-4</sub>alkyl;

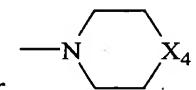
R<sup>3</sup> represents halo; hydroxy; C<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxy-C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6b</sup>R<sup>7b</sup>, -C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -S(=O)<sub>n1</sub>-R<sup>8a</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8a</sup>; C<sub>2-6</sub>alkenyl or C<sub>2-6</sub>alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6b</sup>R<sup>7b</sup>, -C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -S(=O)<sub>n1</sub>-R<sup>8a</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8a</sup>; polyhaloC<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxy-C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6b</sup>R<sup>7b</sup>, -C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -S(=O)<sub>n1</sub>-R<sup>8a</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8a</sup>; C<sub>1-6</sub>alkyloxy optionally substituted with one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxy-carbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6b</sup>R<sup>7b</sup>, -C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -S(=O)<sub>n1</sub>-R<sup>8a</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8a</sup>; polyhaloC<sub>1-6</sub>alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxy-C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6b</sup>R<sup>7b</sup>, -C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6b</sup>R<sup>7b</sup>, -S(=O)<sub>n1</sub>-R<sup>8a</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8a</sup>; C<sub>1-6</sub>alkylthio; polyhaloC<sub>1-6</sub>alkylthio;

$C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkylcarbonyloxy;  $C_{1-6}$ alkylcarbonyl; polyhalo-  
 $C_{1-6}$ alkylcarbonyl; cyano; carboxyl; aryloxy; arylthio; arylcarbonyl;  $NR^{6b}R^{7b}$ ;  
 $C(=O)-NR^{6b}R^{7b}$ ;  $-NR^5-C(=O)-NR^{6b}R^{7b}$ ;  $-NR^5-C(=O)-R^5$ ;  $-S(=O)_{n1}-R^{8a}$ ;  
 $-NR^5-S(=O)_{n1}-R^{8a}$ ;  $-S-CN$ ; or  $-NR^5-CN$ ;

$R^4$  represents hydrogen; halo; hydroxy;  $C_{1-4}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy,  $NR^{10}R^{11}$ ,  $-C(=O)-NR^{10}R^{11}$ ,  $-NR^5-C(=O)-NR^{10}R^{11}$ ,  $-S(=O)_{n1}-R^{12}$  or  $-NR^5-S(=O)_{n1}-R^{12}$ ;  $C_{2-4}$ alkenyl or  $C_{2-4}$ alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy,  $NR^{10}R^{11}$ ,  $-C(=O)-NR^{10}R^{11}$ ,  $-NR^5-C(=O)-NR^{10}R^{11}$ ,  $-S(=O)_{n1}-R^{12}$  or  $-NR^5-S(=O)_{n1}-R^{12}$ ; polyhalo $C_{1-3}$ alkyl;  $C_{1-4}$ alkyloxy optionally substituted with carboxyl; polyhalo $C_{1-3}$ alkyloxy;  $C_{1-4}$ alkylthio; polyhalo $C_{1-3}$ alkylthio;  $C_{1-4}$ alkyloxycarbonyl;  $C_{1-4}$ alkylcarbonyloxy;  $C_{1-4}$ alkylcarbonyl; polyhalo $C_{1-4}$ alkylcarbonyl; nitro; cyano; carboxyl;  $NR^{10}R^{11}$ ;  $C(=O)NR^{10}R^{11}$ ;  $-NR^5-C(=O)-NR^{10}R^{11}$ ;  $-NR^5-C(=O)-R^5$ ;  $-S(=O)_{n1}-R^{12}$ ;  $-NR^5-S(=O)_{n1}-R^{12}$ ;  $-S-CN$ ; or  $-NR^5-CN$ ;

$R^5$  represents hydrogen;  $C_{1-4}$ alkyl or  $C_{2-4}$ alkenyl;

$R^6$  and  $R^7$  each independently represent hydrogen; cyano;  $C_{1-6}$ alkylcarbonyl optionally substituted with  $C_{1-4}$ alkyloxy or carboxyl;  $C_{1-6}$ alkyloxycarbonyl;  $C_{3-7}$ cycloalkylcarbonyl; adamantanylcarbonyl;  $C_{1-4}$ alkyloxy $C_{1-4}$ alkyl;  $C_{1-4}$ alkyl substituted with  $C_{1-4}$ alkyl- $NR^5$ ;  $C_{1-6}$ alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy, polyhalo-

$C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy $C_{1-4}$ alkyloxy,  $NR^{6a}R^{7a}$ ,  $C(=O)NR^{6a}R^{7a}$  or ; with  $X_4$  representing O,  $CH_2$ ,  $CHOH$ ,  $CH-N(R^5)_2$ ,  $NR^5$  or  $N-C(=O)-C_{1-4}$ alkyl;

$R^{6a}$  and  $R^{7a}$  each independently represent hydrogen;  $C_{1-4}$ alkyl;  $C_{1-4}$ alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

$R^{6b}$  and  $R^{7b}$  each independently represent hydrogen; cyano;  $C_{1-6}$ alkylcarbonyl optionally substituted with  $C_{1-4}$ alkyloxy or carboxyl;  $C_{1-6}$ alkyloxycarbonyl;  $C_{3-7}$ cycloalkylcarbonyl; adamantanylcarbonyl;  $C_{1-4}$ alkyloxy $C_{1-4}$ alkyl;  $C_{1-4}$ alkyl substituted with  $C_{1-4}$ alkyl-NR<sup>5</sup>-;  $C_{1-6}$ alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy, polyhalo $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy- $C_{1-4}$ alkyloxy, NR<sup>6c</sup>R<sup>7c</sup> or C(=O)NR<sup>6c</sup>R<sup>7c</sup>;

$R^{6c}$  and  $R^{7c}$  each independently represent hydrogen;  $C_{1-4}$ alkyl or  $C_{1-4}$ alkylcarbonyl;  $R^8$  represents  $C_{1-4}$ alkyl optionally substituted with hydroxy; polyhalo $C_{1-4}$ alkyl or NR<sup>6</sup>R<sup>7</sup>;  $R^{8a}$  represents  $C_{1-4}$ alkyl optionally substituted with hydroxy; polyhalo $C_{1-4}$ alkyl or NR<sup>6b</sup>R<sup>7b</sup>;  $R^9$  represents halo; hydroxy;  $C_{1-6}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>;  $C_{2-6}$ alkenyl or  $C_{2-6}$ alkynyl, each optionally substituted with at least one substituent selected from hydroxy; cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; polyhalo $C_{1-6}$ alkyl;  $C_{1-6}$ alkyloxy optionally substituted with carboxyl; polyhalo $C_{1-6}$ alkyloxy;  $C_{1-6}$ alkylthio; polyhalo $C_{1-6}$ alkylthio;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkylcarbonyloxy;  $C_{1-6}$ alkylcarbonyl; cyano; carboxyl; NR<sup>6</sup>R<sup>7</sup>; C(=O)NR<sup>6</sup>R<sup>7</sup>; -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>; -NR<sup>5</sup>-C(=O)-R<sup>5</sup>; -S(=O)<sub>n1</sub>-R<sup>8</sup>; -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; -S-CN; or -NR<sup>5</sup>-CN;

$R^{10}$  and  $R^{11}$  each independently represent hydrogen;  $C_{1-6}$ alkyl; cyano;  $C_{1-6}$ alkylcarbonyl;  $C_{1-4}$ alkyloxy $C_{1-4}$ alkyl; or  $C_{1-4}$ alkyl substituted with  $C_{1-4}$ alkyl-NR<sup>5</sup>-;

$R^{12}$  represents  $C_{1-4}$ alkyl or NR<sup>10</sup>R<sup>11</sup>;

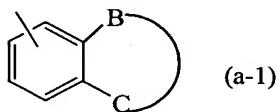
$n1$  represents an integer with value 1 or 2;

aryl represents phenyl or phenyl substituted with at least one substituent selected from halo,  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl,  $C_{1-6}$ alkyloxy, cyano, nitro, polyhalo $C_{1-6}$ alkyl or polyhalo $C_{1-6}$ alkyloxy.

2. (Original) A compound according to claim 1 wherein  
 X represents a direct bond;  $-(CH_2)_{n_3}-$  or  $-(CH_2)_{n_4}-X_a-X_b-$ ;

with  $n_3$  representing an integer with value 1, 2, 3 or 4;  
 with  $n_4$  representing an integer with value 1 or 2;  
 with  $X_a$  representing O or  $NR^5$ ; and  
 with  $X_b$  representing a direct bond or  $C_{1-2}$ alkyl;

$R^2$  represents  $C_{3-7}$ cycloalkyl; phenyl or a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; or a radical of formula



wherein  $-B-C-$  represents a bivalent radical of formula

$-CH_2-CH_2-CH_2-$  (b-1);  
 $-CH_2-CH_2-CH_2-CH_2-$  (b-2);  
 $-X_1-CH_2-CH_2-(CH_2)_n-$  (b-3);  
 $-X_1-CH_2-(CH_2)_n-X_1-$  (b-4);  
 $-X_1-(CH_2)_n-CH=CH-$  (b-5);

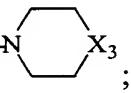
with  $X_1$  representing O or  $NR^5$ ;

$n$  representing an integer with value 0, 1, 2 or 3;

$n'$  representing an integer with value 0 or 1;

wherein said  $R^2$  substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy;  $C_{1-6}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy,  $NR^6R^7$ ,  $-C(=O)-NR^6R^7$ ,  $-NR^5-C(=O)-NR^6R^7$ ,  $-S(=O)_{n1}-R^8$  or  $-NR^5-S(=O)_{n1}-R^8$ ;  $C_{2-6}$ alkenyl or  $C_{2-6}$ alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy,  $NR^6R^7$ ,  $-C(=O)-NR^6R^7$ ,  $-NR^5-C(=O)-NR^6R^7$ ,  $-S(=O)_{n1}-R^8$  or  $-NR^5-S(=O)_{n1}-R^8$ ; polyhalo $C_{1-6}$ alkyl;  $C_{1-6}$ alkyloxy optionally substituted with carboxyl; polyhalo $C_{1-6}$ alkyloxy;  $C_{1-6}$ alkylthio; polyhalo $C_{1-6}$ alkylthio;

$C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkylcarbonyloxy;  $C_{1-6}$ alkylcarbonyl; polyhalo $C_{1-6}$ alkylcarbonyl; cyano; carboxyl;  $NR^6R^7$ ;  $C(=O)NR^6R^7$ ;  $-NR^5-C(=O)-NR^6R^7$ ;  $-NR^5-C(=O)-R^5$ ;  $-S(=O)_{n1}-R^8$ ;  $-NR^5-S(=O)_{n1}-R^8$ ;  $-S-CN$ ;  $-NR^5-CN$ ; aryloxy; arylthio; arylcarbonyl; aryl $C_{1-4}$ alkyl; aryl $C_{1-4}$ alkyloxy; a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5- or 6-membered monocyclic heterocycle optionally being substituted

with at least one substituent selected from  $R^9$ ; or  $-(CH_2)_{n2}-X_2-(CH_2)_{n2}N$  

with  $n2$  representing an integer with value 0, 1, 2, 3 or 4;

with  $X_2$  representing O,  $NR^5$  or a direct bond;

with  $X_3$  representing O or  $NR^5$ ;

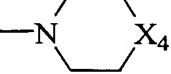
$R^3$  represents halo; hydroxy;  $C_{1-6}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy,  $NR^{6b}R^{7b}$ ,  $-C(=O)-NR^{6b}R^{7b}$ ,  $-NR^5-C(=O)-NR^{6b}R^{7b}$ ,  $-S(=O)_{n1}-R^{8a}$  or  $-NR^5-S(=O)_{n1}-R^{8a}$ ;  $C_{2-6}$ alkenyl or  $C_{2-6}$ alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyloxy,  $NR^{6b}R^{7b}$ ,  $-C(=O)-NR^{6b}R^{7b}$ ,  $-NR^5-C(=O)-NR^{6b}R^{7b}$ ,  $-S(=O)_{n1}-R^{8a}$  or  $-NR^5-S(=O)_{n1}-R^{8a}$ ; polyhalo $C_{1-6}$ alkyl;  $C_{1-6}$ alkyloxy optionally substituted with carboxyl; polyhalo $C_{1-6}$ alkyloxy;  $C_{1-6}$ alkylthio; polyhalo $C_{1-6}$ alkylthio;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkylcarbonyloxy;  $C_{1-6}$ alkylcarbonyl; polyhalo $C_{1-6}$ alkylcarbonyl; nitro; cyano; carboxyl;  $NR^{6b}R^{7b}$ ;  $C(=O)NR^{6b}R^{7b}$ ;  $-NR^5-C(=O)-NR^{6b}R^{7b}$ ;  $-NR^5-C(=O)-R^5$ ;  $-S(=O)_{n1}-R^{8a}$ ;  $-NR^5-S(=O)_{n1}-R^{8a}$ ;  $-S-CN$ ; or  $-NR^5-CN$ ;

$R^5$  represents hydrogen or  $C_{1-4}$ alkyl;

$R^6$  and  $R^7$  each independently represent hydrogen; cyano;  $C_{1-6}$ alkylcarbonyl;

$C_{14}$ alkyloxy $C_{1-4}$ alkyl;  $C_{1-4}$ alkyl substituted with  $C_{1-4}$ alkyl- $NR^5$ ;  $C_{1-6}$ alkyl optionally

substituted with hydroxy, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyloxy, NR<sup>6a</sup>R<sup>7a</sup>, C(=O)NR<sup>6a</sup>R<sup>7a</sup>

or ; with X<sub>4</sub> representing O or NR<sup>5</sup>;

R<sup>6a</sup> and R<sup>7a</sup> each independently represent hydrogen; C<sub>1-4</sub>alkyl; C<sub>1-4</sub>alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

R<sup>6b</sup> and R<sup>7b</sup> each independently represent hydrogen; cyano; C<sub>1-6</sub>alkylcarbonyl; C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl; C<sub>1-4</sub>alkyl substituted with C<sub>1-4</sub>alkyl-NR<sup>5</sup>; C<sub>1-6</sub>alkyl optionally substituted with hydroxy, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyloxy, NR<sup>6a</sup>R<sup>7a</sup> or C(=O)NR<sup>6a</sup>R<sup>7a</sup>;

R<sup>8</sup> represents C<sub>1-4</sub>alkyl, polyhaloC<sub>1-4</sub>alkyl or NR<sup>6</sup>R<sup>7</sup>;

R<sup>8a</sup> represents C<sub>1-4</sub>alkyl, polyhaloC<sub>1-4</sub>alkyl or NR<sup>6b</sup>R<sup>7b</sup>.

3. (Original) A compound as claimed in claim 1 wherein ring A represents phenyl or pyridyl; R<sup>1</sup> represents hydrogen; X represents a direct bond or -(CH<sub>2</sub>)<sub>n3</sub>-; R<sup>2</sup> represents phenyl or a radical of formula (b-4), wherein said R<sup>2</sup> may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, NR<sup>6</sup>R<sup>7</sup>, C(=O)NR<sup>6</sup>R<sup>7</sup>, C<sub>1-4</sub>alkyloxy or C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyloxy; C<sub>1-6</sub>alkyloxy; C<sub>1-6</sub>alkyloxy carbonyl; C<sub>1-4</sub>alkyloxyC<sub>1-6</sub>alkyloxy; cyano; carboxyl; C(=O)NR<sup>6</sup>R<sup>7</sup>; -S(=O)<sub>n1</sub>-R<sup>8</sup>; arylC<sub>1-4</sub>alkyloxy; or a 5- or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5- or 6-membered heterocycle optionally being substituted with at least one substituent selected from R<sup>9</sup>; R<sup>3</sup> represents halo; hydroxy; C<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, NR<sup>6b</sup>R<sup>7b</sup> or C(=O)NR<sup>6b</sup>R<sup>7b</sup>; C<sub>2-6</sub>alkenyl optionally substituted with at least one substituent selected from carboxyl or C<sub>1-4</sub>alkyl-oxycarbonyl; polyhaloC<sub>1-6</sub>alkyloxy; C<sub>1-6</sub>alkyloxy optionally substituted with C<sub>1-4</sub>alkyloxy; C<sub>1-6</sub>alkylthio; C<sub>1-6</sub>alkyloxy carbonyl; C<sub>1-6</sub>alkylcarbonyl; cyano; carboxyl; NR<sup>6b</sup>R<sup>7b</sup>; C(=O)NR<sup>6b</sup>R<sup>7b</sup>; -NR<sup>5</sup>-C(=O)-R<sup>5</sup>; -S(=O)<sub>n1</sub>-R<sup>8</sup>; -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; or -S-CN;

$R^4$  represents hydrogen; halo;  $C_{1-6}$ alkyl; cyano; hydroxy;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkyloxy; carboxyl; or  $NR^6R^7$ .

4. (Currently Amended) A compound as claimed in claim 1 or 3 wherein ring A represents phenyl or pyridyl;  $R^1$  represents hydrogen; X represents a direct bond;  $R^2$  represents phenyl wherein said  $R^2$  may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo;  $C_{1-6}$ alkyl substituted with one substituent selected from hydroxy, cyano,  $NR^6R^7$ ,  $C(=O)NR^6R^7$ ,  $C_{1-4}$ alkyloxy or  $C_{1-4}$ alkyloxy $C_{1-4}$ alkyloxy;  $C_{1-6}$ alkyloxy;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-4}$ alkyloxy $C_{1-6}$ alkyloxy;  $C(=O)NR^6R^7$ ;  $-S(=O)_{n1}-R^8$ ; or a 5-or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered heterocycle optionally being substituted with at least one substituent selected from  $R^9$ ;  $R^3$  represents halo; hydroxy;  $C_{1-6}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,  $C_{1-4}$ alkyloxy,  $NR^{6b}R^{7b}$  or  $C(=O)NR^{6b}R^{7b}$ ;  $C_{2-6}$ alkenyl optionally substituted with at least one substituent selected from carboxyl or  $C_{1-4}$ alkyloxycarbonyl; polyhalo $C_{1-6}$ alkyloxy;  $C_{1-6}$ alkyloxy optionally substituted with  $C_{1-4}$ alkyloxy or  $NR^{6b}R^{7b}$ ;  $C_{1-6}$ alkylthio;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkylcarbonyl; cyano; carboxyl;  $NR^{6b}R^{7b}$ ;  $C(=O)NR^{6b}R^{7b}$ ;  $-S(=O)_{n1}-R^8$ ;  $-NR^5-C(=O)-R^5$ ; or  $-NR^5-S(=O)_{n1}-R^8$ ;  $R^4$  represents hydrogen; halo;  $C_{1-6}$ alkyl; hydroxy;  $C_{1-6}$ alkyl-oxycarbonyl;  $C_{1-6}$ alkyloxy; carboxyl; or  $NR^6R^7$ .

5. (Currently Amended) A compound as claimed in claim 1 any one of claims 1 to 4 wherein the  $R^3$  substituent is linked to ring A in meta position compared to the  $NR^1$  linker.

6. (Currently Amended) A compound as claimed in claim 1 any one of claims 1 to 4 wherein the  $R^3$  substituent is linked to ring A in para position compared to the  $NR^1$  linker.

7. (Currently Amended) A compound as claimed in claim 1 any one of claims 1 to 6 wherein  $R^3$  represents  $NR^{6b}R^{7b}$ .

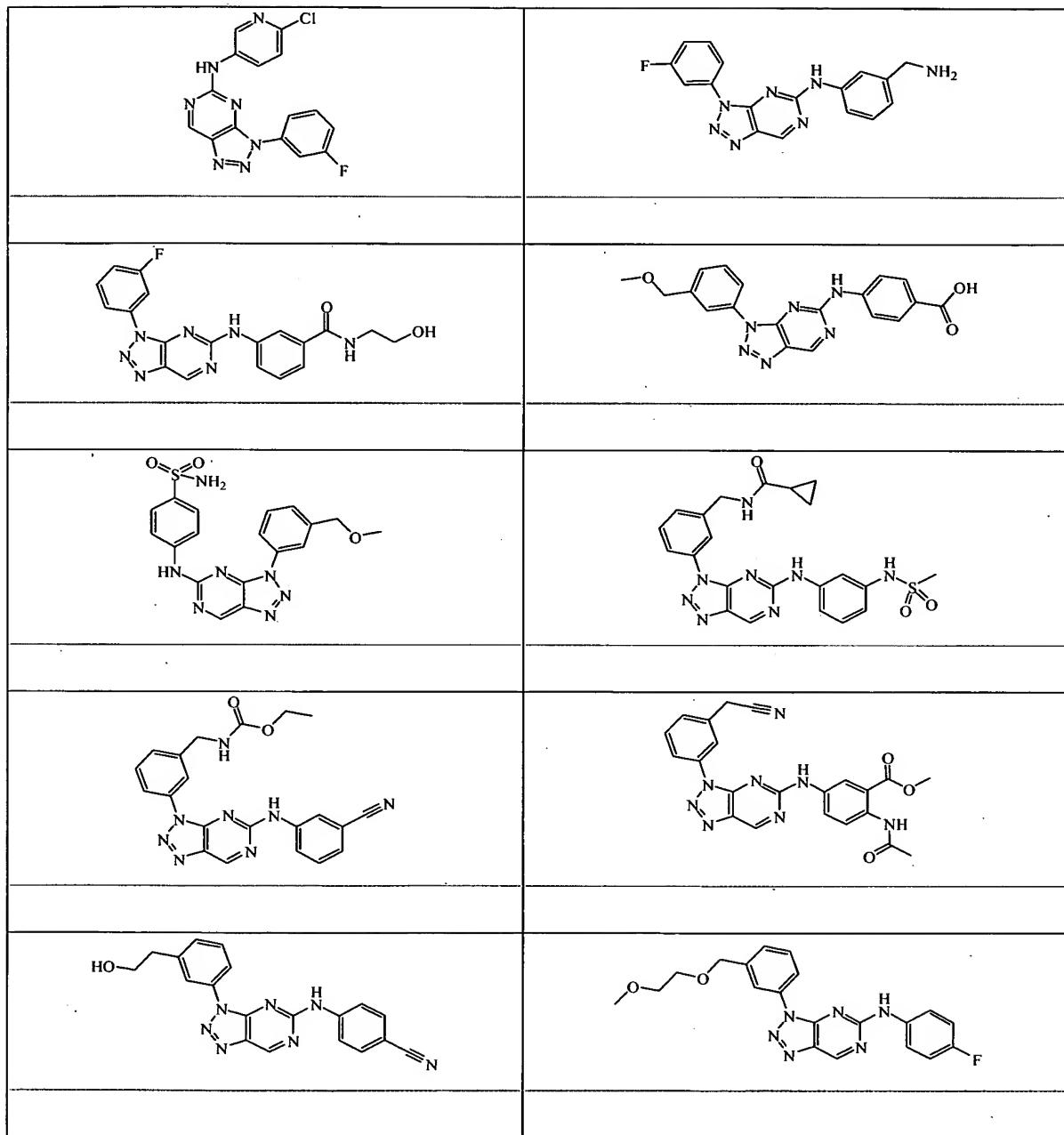
8. (Currently Amended) A compound as claimed in claim 1 ~~any one of claims 1 to 7~~ wherein X represents a direct bond.

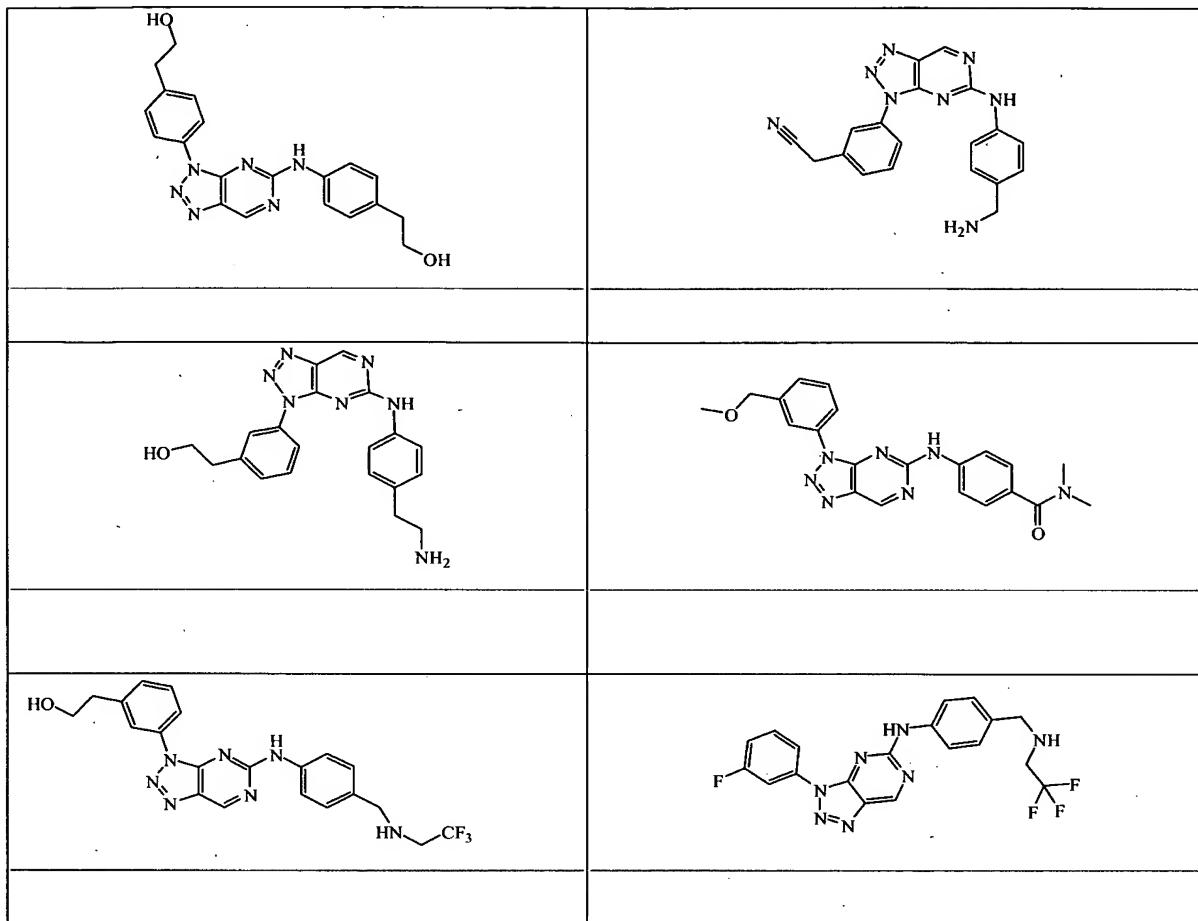
9. (Currently Amended) A compound as claimed in claim 1 ~~any one of claims 1, 5 to 8~~ wherein R<sup>2</sup> represents C<sub>3-7</sub>cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1) wherein said R<sup>2</sup> substituent is substituted with at least one substituent selected from C<sub>1-6</sub>alkyl substituted with NR<sup>6</sup>R<sup>7</sup>; C<sub>2-6</sub>alkenyl or C<sub>2-6</sub>alkynyl, each substituted with NR<sup>6</sup>R<sup>7</sup>; polyhaloC<sub>1-6</sub>alkyl substituted with NR<sup>6</sup>R<sup>7</sup>; C<sub>1-6</sub>alkyloxy substituted with NR<sup>6</sup>R<sup>7</sup>; polyhaloC<sub>1-6</sub>alkyloxy substituted with NR<sup>6</sup>R<sup>7</sup>; or NR<sup>6</sup>R<sup>7</sup>.

10. (Currently Amended) A compound as claimed in claim 1 ~~any one of claims 1, 5, 6, 8 or 9~~ wherein R<sup>3</sup> represents C<sub>1-6</sub>alkyl substituted with NR<sup>6b</sup>R<sup>7b</sup>; C<sub>2-6</sub>alkenyl or C<sub>2-6</sub>alkynyl, each substituted with NR<sup>6b</sup>R<sup>7b</sup>; polyhaloC<sub>1-6</sub>alkyl substituted with NR<sup>6b</sup>R<sup>7b</sup>; C<sub>1-6</sub>alkyloxy substituted with NR<sup>6b</sup>R<sup>7b</sup>; polyhaloC<sub>1-6</sub>alkyloxy substituted with NR<sup>6b</sup>R<sup>7b</sup>; or NR<sup>6b</sup>R<sup>7b</sup>.

11. (Currently Amended) A compound as claimed in claim 1 ~~any one of claims 1, 5, 6, 7, 8 or 10~~ wherein R<sup>2</sup> represents C<sub>3-7</sub>cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1), wherein said R<sup>2</sup> substituent is substituted with at least one substituent selected from halo; polyhaloC<sub>1-6</sub>alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxy-C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>; polyhalo-C<sub>1-6</sub>alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkyloxy-C<sub>1-4</sub>alkyloxy, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyloxy, NR<sup>6</sup>R<sup>7</sup>, -C(=O)-NR<sup>6</sup>R<sup>7</sup>, -NR<sup>5</sup>-C(=O)-NR<sup>6</sup>R<sup>7</sup>, -S(=O)<sub>n1</sub>-R<sup>8</sup> or -NR<sup>5</sup>-S(=O)<sub>n1</sub>-R<sup>8</sup>.

12. (Currently Amended) A compound as claimed in claim 1 wherein the compound is selected from the group consisting of





a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereoisomeric form thereof.

13. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound as claimed in of claim 1 any one of claims 1 to 12 for use as a medicine.

14. (Currently Amended) The use of a compound as defined in any one of claims 1 to 12 for the manufacture of a medicament A method for the prevention or the treatment of diseases a disease mediated through GSK3 comprising administering a therapeutically

effective amount of a compound of claim 1 to a patient in need of treatment for a disease mediated through GSK3.

15. (Currently Amended) The method use of a compound as defined in any one of claims 1 to 12 for the manufacture of a medicament for the prevention or the treatment of a disease mediated through GSK3 of claim 14 wherein the disease is selected from the group consisting of bipolar disorder (in particular manic depression), diabetes, Alzheimer's disease, leukopenia, FTDP-17 (Fronto-temporal dementia associated with Parkinson's disease), cortico-basal degeneration, progressive supranuclear palsy, multiple system atrophy, Pick's disease, Niemann Pick's disease type C, Dementia Pugilistica, dementia with tangles only, dementia with tangles and calcification, Downs syndrome, myotonic dystrophy, Parkinsonism-dementia complex of Guam, aids related dementia, Postencephalic Parkinsonism, prion diseases with tangles, subacute sclerosing panencephalitis, frontal lobe degeneration (FLD), argyrophilic grains disease, subacute sclerotizing panencephalitis (SSPE) ( late complication of viral infections in the central nervous system), inflammatory diseases, depression, cancer, dermatological disorders, neuroprotection, schizophrenia, and pain.

16. (Currently Amended) The method use of a compound as claimed in claim 14 for the prevention or the treatment of a disease mediated through GSK3 of claim 14 wherein the disease is selected from the group consisting of Alzheimer's disease; diabetes; cancer; inflammatory diseases; bipolar disorder; depression; and pain.

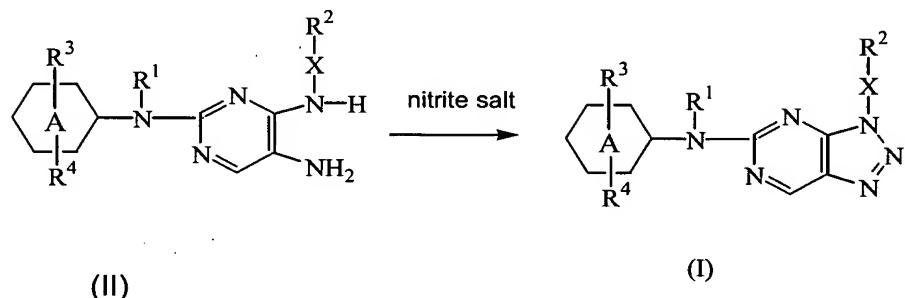
17. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredient a therapeutically effective amount of a compound as claimed in claim 1, any one of claims 1 to 12.

18. (Currently Amended) A process for preparing a pharmaceutical composition as claimed in claim 17 characterized in that a therapeutically effective amount of a compound as claimed in claim 1 any one of claims 1 to 12 is intimately mixed with a pharmaceutically

acceptable carrier.

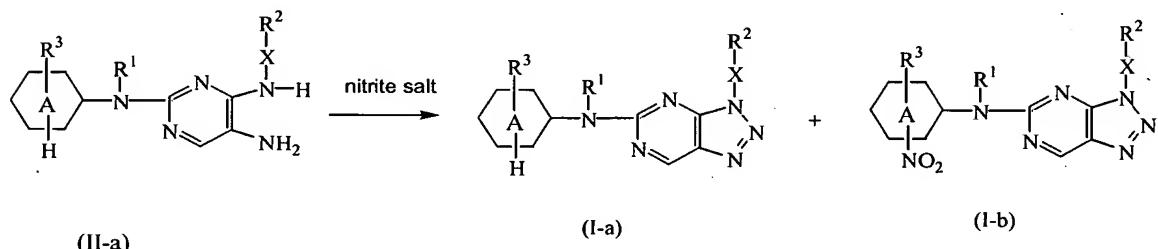
19. (Original) A process for preparing a compound as claimed in claim 1, characterized by

a) by cyclizing an intermediate of formula (II) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



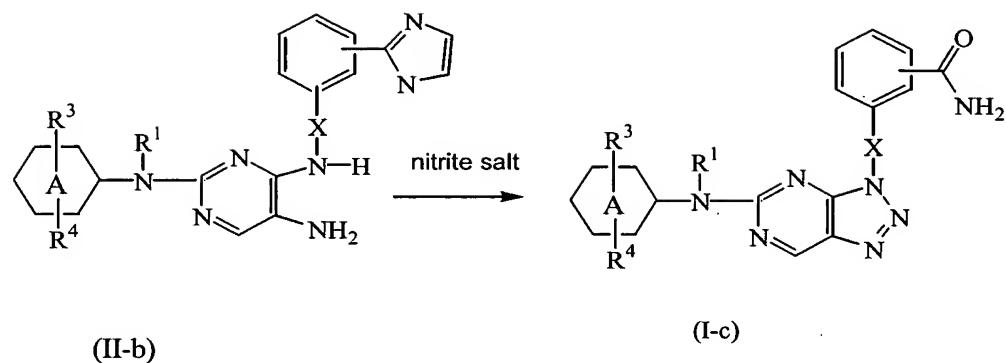
wherein ring A, R<sup>1</sup> to R<sup>4</sup> and X are as defined in claim 1;

b) cyclizing an intermediate of formula (II-a) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



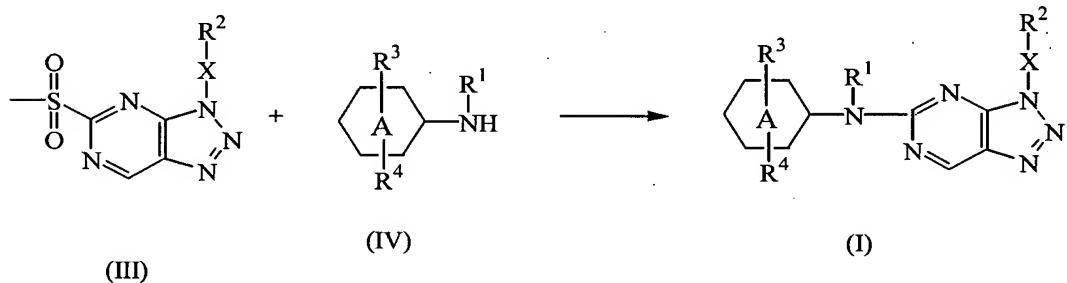
wherein ring A, R<sup>1</sup> to R<sup>3</sup> and X are as defined in claim 1;

c) cyclizing an intermediate of formula (II-b) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,



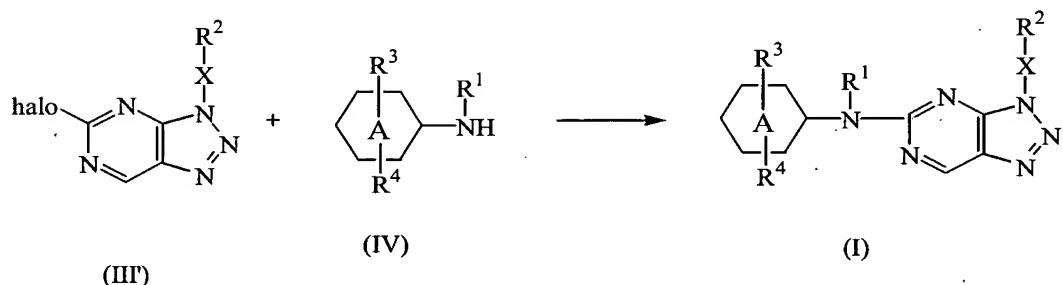
wherein ring A,  $R^1$ ,  $R^3$ ,  $R^4$  and X are as defined in claim 1;

d) reacting an intermediate of formula (III) with an intermediate of formula (IV) in the presence of a suitable solvent,



wherein ring A, R<sup>1</sup> to R<sup>4</sup> and X are as defined in claim 1;

e) reacting an intermediate of formula (III') with an intermediate of formula (IV) in the presence of a suitable solvent, and optionally in the presence of a suitable base,



or, if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely,

converting the acid addition salt form into the free base by treatment with alkali, or  
converting the base addition salt into the free acid by treatment with acid; and, if desired,  
preparing stereochemically isomeric forms, quaternary amines or *N*-oxide forms thereof.